

NITROSO COMPOUNDS I. THE REACTION OF PHENYLCOPPER REAGENTS

WITH NITROSAMINES. (CLEAVAGE OF THE N-N BOND)

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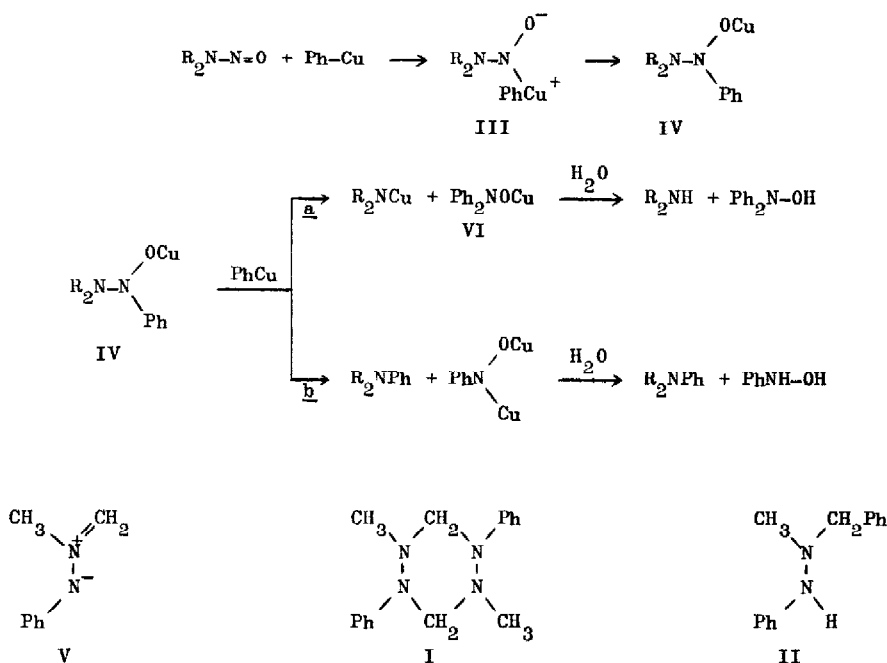
Because of the recently expressed interest in the chemistry of nitrosamines for their carcinogenic¹ and chemotherapeutic² properties as well as their use in organic synthesis³⁻⁵, we thought it interesting to study some of their reactions with organo-metallic reagents. Phenyllithium and phenylmagnesium bromide react with dialkylnitrosamines to produce sym-hexahydropyridazines (I)^{4,5} and N,N'-diphenyl-N-methylhydrazine (II)⁶⁻⁸ respectively as the principal products in which the N-N bonds of the nitrosamines remained unaffected. By contrast we have observed that phenylcopper reagents react with nitrosamines to give products resulting from the cleavage of the N-N bonds.

In a representative reaction when 1.1 equivalents of phenylcopper⁹ (prepared from equimolar amounts of phenylmagnesium bromide and copper(I) chloride in THF) reacted with one equivalent of dimethylnitrosamine (DMNA) at -20° for 3 hr, the following products¹⁰ (% yields in brackets) were obtained subsequent to the usual work-up¹¹: dimethylamine (51), biphenyl (13), diphenylamine (29), diphenylhydroxylamine (30), phenol (20) and traces of β -phenylhydroxylamine and N,N-dimethylaniline. In the above reaction if diphenylnitrosamine (DPNA) was used in place of DMNA then the following products were obtained: diphenylamine (44), diphenylhydroxylamine (28), phenol (21) and traces of triphenylamine and β -phenylhydroxylamine. In neither reaction was I or II formed. The reactions of DMNA and DPNA with bromomagnesium diphenylcuprate¹¹ (prepared

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from two equivalents of phenylmagnesium bromide and one equivalent of copper(I) chloride in THF) follow a similar course to that observed with phenylcopper reagent.

We are still working on the mechanism of the reaction but we feel that the following sequence (as exemplified by phenylcopper¹²) may explain the formation of various products :



The intermediate IV has probably been formed by a direct nucleophilic attack by the organocopper cluster on the nitroso nitrogen to form III followed by the transfer of a phenyl group. Alternatively, an electron-transfer process similar to the one proposed by House and Umen^{13,14} for the formation of an enolate ion during the reaction of cuprates with α,β -unsaturated carbonyl compounds may explain the formation of the adduct IV. An intermediate like IV with Li or MgBr in place of Cu is believed to be involved in the reaction of nitrosamines with either phenyllithium^{4,5} or phenylmagnesium bromide⁶⁻⁸. This type of intermediate (i.e., the one with lithium or bromomagnesium in place of copper in IV) undergoes an elimination reaction to give a dipolar species e.g., V (for R = CH₃ in IV) which reacts further to give the observed products

I or II. But IV does not seem to undergo the elimination reaction, at least not so fast probably because copper is less electropositive than either lithium or magnesium. Thus a second molecule of phenylcopper has an opportunity to react with IV probably involving a multi-centre transition state and cleave the N-N bond. Since R_2NH and Ph_2N-OH were the main products probably for both steric and electronic reasons, pathway a is obviously of major importance. The biphenyl, formed in the reaction of DMNA with phenylcopper, has probably originated from the oxidative coupling of the latter. (The reduction potential of DMNA is less negative than -1.0 vs sce¹⁵ and therefore like nitrobenzene it is expected to oxidise^{14,16} the copper reagent). Biphenyl was not formed in the analogous reaction of DPNA. The reason for this is unclear at the moment although the steric factor may be involved. All the diphenylamine from the reaction of DMNA with phenylcopper and at least half of that formed in the analogous reaction with DPNA, and phenol (in both cases) have probably been formed by an exchange reaction between VI and a molecule of phenylcopper. A similar exchange reaction has been proposed to explain the formation of diphenylamine and phenol in the reaction of diphenylhydroxylamine and excess phenylmagnesium bromide^{6a, 17}.

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17. See also P. Buck and G. Kobrich, *Tetrahedron Lett.*, 1967, 1563, this paper proposes reverse addition of PhLi to Ph-N=O to give $\text{Ph-N(I}_1\text{)-O}^-\text{Ph}$ which reacts further with another molecule of PhLi to give Ph_2NL_1 and PhOL_1 , but no nitrosobenzene seemed to have formed in our system. Furthermore, we did not think PhCu had added to $\text{R}_2\text{N-N=O}$ in a "reverse" manner because no $\text{R}_2\text{N-NHPh}$ was formed.